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## **Health economic changes as a result of implementation of targeted therapy for metastatic renal cell carcinoma**

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# Hepatic encephalopathy treatment and its effect on driving abilities: A continental divide

## To the Editor:

We read with great interest the review article on hepatic encephalopathy (HE) that, in addition to the recent EASL/AASLD guidelines, is informative about the spectrum of this disease [1,2]. We set out to evaluate the practice patterns of clinical HE experts worldwide (285 ISHEN members and authors of clinical HE articles in the last 5 years) through a systematic electronic questionnaire focused on the management and effect on driving ability in HE. Results are summarized in the Table 1.

Response rate was 35%. Respondents were from 23 different countries in 4 different continents (Europe: n = 48, Americas n = 28, Asia: n = 21). Sixty per cent specialized in hepatology and most had more than 10 years of clinical experience. Management of overt HE (OHE) is similar between continents and complies with guidelines, although medical management differs in some aspects: in the US rifaximin is used as much as lactulose (by 96%) but in Europe and Asia branched chain amino acids (BCAA) and L-ornithine L-aspartate (LOLA) respectively are preferred after lactulose. This could be due to the unavailability of LOLA and BCAA in the US. On the other hand <1% from Europe report probiotic use compared with 20% in the US and Asia, which could reflect real-practice differences. Interestingly, while clinical impression is used to assess treatment efficacy in most respondents, only 4% of US-based clinicians used blood ammonia levels in contrast to their European and Asian counterparts.

## Diagnosis and treatment of covert HE

Sixty percent of clinicians engage in some form of covert HE (CHE) screening procedure. However, only 1/10 refer the majority of patients for formal screening. Most clinicians focus screening efforts on select patient sub-groups: prior overt HE, specific cognitive complaints from caregiver or patient, and patients' quality of life (QoL) issues being the major reasons for screening referral. As found by others, Portosystemic Encephalopathy Syndrome Test (PSE) is the preferred psychometric test (41%) along with Critical Flicker Frequency (CFF) (37%) [3]. As expected there are intercontinental differences: PSE is Europe's favoured test whereas the Stroop EncephalApp and CFF are preferred in America and Asia, respectively. Interestingly, systematic QoL assessment is widely used (40%) indicating that the established close link between

CHE and QoL, albeit tempered by its relationship with cirrhosis severity, is being strongly considered in clinical practice. Most clinicians report that they initiate CHE treatment (with the same drugs as in OHE) on a case-to-case basis but when asked to recount cases that were started on CHE treatment in the last month <5% of those fulfilling local CHE criteria were treated. This could reflect the gap between knowledge, attitudes and the ultimate translation into practice. The respondents felt that there were still a wide range of unanswered questions regarding CHE management. Importantly, the 40% who do not engage in CHE screening are reluctant for several reasons: 43% find screening too time consuming and a similar proportion finds that lack of consensus and trained personnel hinders screening efforts. These obstacles seem to be most pronounced in America but have seemingly diminished since 2007 where a similar query was done [4].

## HE and traffic safety

Several studies have shown that HE patients may have difficulties with driving and a convincing 99% agree that covert and recent overt HE impact on driving skills. Respondents answered driving-related questions in accordance with their local driving regulations. We found that only 1/5 of the respondents translated this issue into practice and asked >60% of patients about driving history, often recommending driving restrictions. On the other extreme a similar proportion ask <5% of patients. Most used clinical impression to categorize patients as unsafe drivers, however some also considered traffic history (45%), psychometric test results (40%), time since OHE (38%), and caregivers opinion (37%) in making this judgement. Overall, 79% had at some point urged patients with recent OHE (<3 months) and 67% with CHE not to drive; but during the past month driving restrictions had been recommended in very few patients. In case of any prior, currently controlled OHE even fewer would recommend driving restrictions. This inconsistency between knowledge and practice reflects the fact that 75% of respondents find it difficult to deal with traffic safety issues and only half are aware of local laws which were also interpreted differently.

In this survey of clinical investigators interested in HE, 60% of respondents offer screening for the presence of CHE via different

## Letters to the Editor

**Table 1. Systematic electronic questionnaire focusing on the management and effect on driving ability in HE patients.**

	All	Europe	Americas	Asia
<b>Covert HE management</b>				
Offers screening for covert HE	59%	56%	54%	71%
Preferred screening tools*	QoL + PSE	QoL + PSE	QoL + Stroop test	QoL + PSE/CFF
Treatment of CHE was offered:				
On case-to-case basis	58%	51%	65%	62%
Never	12%	16%	14%	5%
Always	30%	33%	22%	33%
Drugs used to treat CHE:				
Lact/rifax/BCAA/probiotics/LOLA (%)*	94/53/21/15/15	79/42/31/6/10	79/57/0/21/11	85/43/14/19/24
Did not offer screening for CHE	41%	44%	46%	29%
For those who do not offer screening, the following reasons were stated:				
Lack of time*	43%	22%	78%	35%
Lack of consensus on which tests to use*	38%	27%	54%	35%
Lack of personnel*	41%	34%	69%	0%
Lack of consensus about consequences of screening	44%	39%	54%	35%
I don't think it is important	0%	0%	0%	0%
<b>HE and traffic safety</b>				
Finds it difficult to deal with traffic issues and HE	75%	75%	86%	62%
Obtains traffic history in majority of cases	21%	17%	29%	14%
Are aware of local driving laws in relation to HE	47%	50%	32%	57%
Thinks recent OHE and CHE impacts driving skills	99%	99%	98%	96%
Will restrict driving in				
Recent OHE	79%	80%	79%	76%
CHE	67%	67%	46%	76%
Prior, currently controlled HE	48%	42%	57%	52%
Recommended driving restrictions in majority of cases of				
Recent OHE (<3 months)	20%	15%	21%	24%
CHE	9%	5%	7%	19%
Prior, currently controlled OHE	7%	6%	0%	14%
Categorizes pts as unsafe driver on the basis of specialized tests apart from clinical impression*	40%	54%	21%	29%

Pts, patients; HE, hepatic encephalopathy; CHE, covert hepatic encephalopathy; OHE, overt hepatic encephalopathy; QoL, quality of life; MELD, model for end stage liver disease; BCAA, branched chain amino acids; LOLA, L-ornithine L-aspartate; PSE, portosystemic encephalopathy syndrome test; CFF, critical flicker frequency.

\*Different between continents.

regional strategies: QoL assessment appears to be widely used in combination with psychometric tests. However, only a few fulfilling local CHE criteria are offered treatment and lack of time, personnel and consensus on key issues appear to be major obstacles. The majority agree that recent and covert HE impact driving skills but only a sub-group of HE experts seem to be addressing this in daily clinical practice. Further clinical studies are needed to engage the non-HE expert audience and answer the important remaining questions.

### Conflict of interest

The authors who have taken part in this letter to the editor declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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